Christina Chan

United States Patent and Trademark Office

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Date: November 1, 2008

Subject: Concerns about prior art for Patent # US 7,241,443, any continuation in part, and Division No. 091616,843

Dear Christina Chan:

I recently received a letter from your office regarding a current patent application based on my technology. Unfortunately, I lost your letter with the correct application numbers and which continuation-in-part patents you were referring to. I am writing this document as a concerned inventor and one trained in the art to point out what I feel are documents indicating that there is prior art for this application as well as for the primary patent I wrote in 1999. I suggest that you take a very close look at the data provided to show that in fact this application is unique.

As one trained in the art as a scientist and inventor I have studied avian immunology for over forty years. In the late 60's, I was trained by Dr. Albert Benedict. He trained me to actively immunizing chickens including egg laying hens, mice, rats, frogs fish, horses, cattle, dogs, cats, rabbits (wild and domestic), pigs, and later actually taught courses on development of monoclonal antibodies from rats and mice. From that I learned that the immunoglobulins from one animal can be used on other animals through passive immunity challenge tests. For poultry, I have training in 1) selecting and raising different strains of poultry, 2) care and use of same, 3) selection of antigens to used to immunize the animals, 4) purification and isolation of specific immunogens to produce specific unique responses by the animals, 5) calculation of dosage for the proper immunogens, 6) selection and determination of the proper injection schedule, 7) proper techniques for injection of immunogens in chickens, 8) proper collection and processing of the eggs or serum, and 9) proper processing of the materials to give unique specific reactions. These methods become general common knowledge in the art for any scientist with advanced work with chickens. These concepts have to be taken into consideration when determining the general common knowledge in the art of making immunogens, injecting egg laying hens and the timing and making of egg based products using the same in the commercial market.

General Common Knowledge in the ART:

Link, K.P. US Patent 2,607,716, Aug. 19, 1952 Prophylactic Composition for Scours: Composition of matter.

They teach about the problem with scours and reference a paper; Smith, T. and R.B. Little, J. Exp. Med. 30: 181 1922. They teach about the treatment of choice using prophylaxis bovine colostrums. They also teach the use of antibacterial serum as a passive treatment. The use of oral delivery is given as the method of choice. Clearly, anyone trained in the art and working with egg yolk antibodies would be aware of this delivery system. This can be delivered spray dried or freeze-dried and serum can be collected from an abattoir.

Peterson; W.E. and B. Campbell, US 3,376,198 Apr.2, 1968, Method of Producing Antibodies in Milk.

They teach the need to select the right antigens and route of injection for immunization of the animals very carefully. They teach the use of pasteurization of the serum products A concept that is carried over into the field is the need to determine the therapeutic significant concentration of the antibodies to give the animal protection. They refer to major organisms such as Staphylococcus aureus and Streptococcus spp. They use Salmonella pullorum and Salmonella typhimurium as the model organisms for making antigens. They imply that "Chickens as a species are far removed from the cow, yet the protective principle produced in the cow is readily conveyed by the milk into the blood stream of the chickens by absorption through the digestive tract". Example #7 demonstrates the use of chickens for passive immunity studies.

Linggood, M.A., P. Porter, and J.R. Powell, US 4,971,794, Nov. 20, 1990. Production of Antibodies Using a Mixture of Strains of E. coli collectively Expressing Type1 Pili, CFA I Pili, CFA II and K88 Pili.

They teach a series of concepts from making antigens with pili structures of the bacterial cell, to types of immunoglobulins formed, and need to obtain substantial quantities of appropriate immunoglobulins for delivery. They discuss the use of the immunoglobulins in human adults and children to prevent or treat gastro-enteric disorders. They point the need to carefully grow the organism under the proper conditions to get the proper antigens.

The following is prior art that is general common knowledge in the art :

Kenny, K. and M. Herzberg, 1967, Early Antibody response in Mice to Either Infection or Immunization with Salmonella typhimurium, J. Bacteriology 93(3): 773-778.

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They teach one how to make standard antigens either heat–killed or living cell vaccines. They teach how to immunize the animals and then how to run passive immunity challenge tests. These are the standard methods without making bacterins. This knowledge was easily transferred to chickens and egg laying hens.

Badakhsh, F. and M. Herzberg, 1969, Deoxycholate-treated, Nontoxic, Whole-Cell Vaccine Protective Against Experimental Salmonellosis of Mice, J. Bacteriology 100(2): 738-744.

This paper teaches how to make group specific antigens and vaccinate animals with it. If this unique method is not followed for the patents listed above, the vaccines become standard whole cell vaccines and are not unique or do they give unique antibodies.

I was trained by Dr. Mendel Herzberg on the development of unique, specific immunogens for stimulating specific selective antibodies to selected immunogens. This includes the development of bacterins that contain unique attachment sites that will bind to wild type antigens and thus can be used for passive protection. Combining these subcellular materials with the proper injection schedule one has the state of the art immunogens to produce antibodies that are not produced with other techniques. I studied the prior art in the form of articles and patents before developing the schedule in the original patent (US #7,241,443 and related patents). If one does not follow the protocols listed in the original patent or does not follow the four week injection schedule or does not follow the concentrations used in ratio's for each dose, then a whole series of patents have been infringed.

In the 60's, Dr. Albert Benedict wrote a whole series on how to make immunogens and vaccinate chickens. It was his classic paper on chicken immunoglobulins that lead to the discovery of carbohydrate on IgG and its use for transportation across plasma membranes. His graduate student Dr. Gerry Leslie was the one that named the yolk immunoglobulin, IgY. It was Polson in the 80's that wrote a series of patents on the making of immunogens and injecting them in chickens.

Dressman, J.C. and A.A. Benedict, 1965, Properties of papain-digested chicken 7S γ-globulin, J. Immunol. 95(5): 855-866.

Benedict, A.A. 1967, Production and purification of chicken immunoglobulins, In: Methods in Immunology and Immunochemistry, Vol 1. Williams, C.A. and M.W. Chase, eds. Academic Press, NY: pages 229-237.

Leslie, G.A. and L.W. Clem, 1969, Phylogeny of immunoglobulin structure and function, J. Exp. Med. 130(6): 1337-1352.

Under the original patent, the way the immunogens were produced is a key to the uniqueness of the patented material. Commercial vaccines are made with the standard of growing the organism as a specific strain, fixing it or using a modified live organism and make the vaccine product. If one uses a commercial killed vaccine or modified live and follows my protocol then there must be processing of the material to get the right, unique immunogen. If there is no processing or just fixing of the organism, then one is infringing on a series of patents some of which I will list later in this document.

In 1998, the CAMAS non-scientists were warned on the possible infringement of current patents if they did not follow the advice given above. They had to make their immunogens or vaccinating antigens in a different way than taught in Polson's patent US #4,357,272, November 2, 1982, Polson's patent US #4,550,019; Tokoro's patent US# 5,080,895, Tsuda et al PCT Patent 0 503 293 A1, Stolle's patent, and others.

The following may be considered as prior art that was available in 1997 when the application was originally written:

Ikemori, Y., M. Kuroki, R.C. Peralta, H. Yokayama, and Y. Kodama, 1992, Protection of neonatal calves against fatal enteric colibacillosis by administration of egg yolk powder from hens immunized with K99-piliated enterotoxigenic Escherichia coli, Am. J. Vet. Res. 53(11): 2005-2008.

They teach how to select microbes, how to develop pili antigens and how to immunize chickens. As to common knowledge, anyone that claims to know about chicken antibodies and how to use them for passive immunization to protect cattle will know this method and use of egg laying chickens. Clearly, this could be carried over to other animals including humans.

Yokoyama, H., R.C. Pera;ta, R. Diaz, S. Sendo, Y. Ikemori and Y. Kodama, 1992, Passive Protective Effect of Chicken Egg Yolk Immunoglobulins against Experimental Enteroxigenic Escherichia coli Infection in Neonatal Piglets, Infect. & Immunity 60(3): 998-1017.

They teach how to select pili antigens and immunize egg laying hens. They collect the egg yolk and teach how to extract it and then use it to passively protect piglets. Again anyone that claims to be trained in the art, should be aware of this paper and what they teach.

Van Donkersgoed, J., C. Guenther, B.N. Evans, A.A. Potter, and R.J. Harland, 1995, Effect of various vaccination protocols on passive and active immunity to Pasteurella haemolytica and Haemophilius somnus in beef calves, Can. Vet. J 36: 424-429.

They teach how to make antigens for vaccination both for passive and active immunity stimulation in cattle. This would be prior art for any passive immunity for respiratory

infections. Unless the immungens are made according to what is taught in the primary patent, they are infringing on other patents.

Davidson, G.P., 1996, Passive Protection Against Diarrheal Disease, J.P.G.N. 23(3): 207-212.

This is one review that only those trained in the art could tie together vaccinations and passive immunity for protection against diarrheal disease.

Bogstedt, A.K., L. Hammarstrium, and A.K. Robertson, 1997, Survival of Immunoglobulins from Different Species through the Gastrointestinal Tract in Healthy Adult Volunteers: Implications for Human Therapy, Antimicrobial Agents and Chemotherapy 41(10): 2320.

This paper is very important for the state-of-the-art in the oral delivery of immunoglobulins for humans and the use of passive immunity. They teach that it does not matter what type of Igg is used whether bovine or chicken IgY, they can be delivered by the oral route and the Igg's will survive the GI tract.

Weltzin, R. and T.P. Monath, 1999, Intranasal Antibody Prophylaxis for Protection against Viral Disease, Clinical Microbiology Rev. 12(3): 383-393.

They teach that antibodies can be used as passive parenteral immunization using intranasal administration. This is common knowledge in the art of passive immunization for viral infections of the upper respiratory system. This article must be read if trained in the current art in using intranasal appliations.

On May 16, 2005, I discovered that in fact the lab assistants and non-scientists at CAMAS had not followed my protocols when making the immunogens. They took short cuts on growing up the microbe, fixing it and making the vaccines. This calls into account the accuracy of the data reported in the first and continuation-in-part of future patents based on this technology. This clearly would be abandonment of the original patent. In September, 2007, the non-scientists informed the vaccination crew that they had changed the immunogens using only fixed not processed antigens. In addition, they did not use the same ratio's of concentrates of the antigen for each injection. Thirdly, they went to schedule of injection every three weeks. Clearly, this copies the method taught by Dr. Klemperer in 1893. It copies Polson's patent of 1985 and infringes on a series of current patents. Clearly, this protocol that they follow does not make unique antibodies but duplicates what is already done by a series of commercial companies.

There are at least eight commercial companies in the US that immunize chickens and make egg yolk based produces. These products are sold for feed additives for cattle, pigs, dogs, poultry and other animals. There are even similar products produced for human consumption. A number of these companies have provided me with some of the marketing brochures. In these

documents, they reference Klemperer paper as prior art that is over 100 years old. They point to Yamamoto et al (1997) book for vaccinating chickens. Simon's patent (2001) covers the use of immunoglobulins for nasal sprays. At least one company uses this for delivery of egg proteins to dogs. This is delivered in the form of a gel spray.

Klemperer, F. 1893, Ueber naturliche Immunitat und ihre Verwerthung fur die Immunisierybgstherapie. Archiv fur Exp pathol Pharmakol 31:356-382.

He teaches that chickens can be vaccinated and the eggs collected from egg laying hens. He taught the use of repeated injections using increasing concentrations of pathogenic whole cultures. He taught to collect the eggs after 4 weeks and extract the egg yolk from the egg. This was then used in passive immunity challenge studies that the antibodies would protect mice.

Yamamoto, T., L.R. Juneja, H. Hatta, and M. Kim, Hen Eggs: their Basic and Applied Science, 1997, CRC Press, Washington D.C. 204 pages. Chapter 11: Egg Yolk Antibody IgY and Its Application, by H. HATTA, m. Ozeki, and K. Tsuda, pages 151-178.

They teach the differences in vaccination of chickens (egg laying hens) and other animals such as rabbits. This review is very good background for anyone starting in the field. They cover the concept of passive immunity of the hen. Any one trained in the art, can carry these concepts over to other animals. As one trained in the art, it is clear to me if one does not follow my methods for making the immunogens (bacterin's) and the injection schedule, they are following the standard methods as give in this and other articles and patents. Therefore, the end products are no more unique than nature's production of the same antibodies. Clearly, this is not new and unique.

Simon, M.R. 2001, US6,932,967, Human medical treatment by aerosol inhalation of immunoglobulin A, 14 pages

Common knowledge in the art is taught about the use of human plasma processed to isolate IgA. The IgA is used in a inhaler or nebulizer to deliver the aerosol administration. This is prior art to nasal spray patents.

I would strongly suggest that your office take a very close look at this prior art before determining whether to issue this application as new and unique? If you have questions, I can be reached at # 952-843-8466,

Sincerely yours,

Peter Nash

Peter Nash PhD